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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/668,496	09/24/2003	Arthur M. Brown	CIINT-0007	7931

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EXAMINER	
DUNSTON, JENNIFER ANN	
ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 07/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/668,496	BROWN ET AL.	
	Examiner	Art Unit	
	Jennifer Dunston	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-51* is/are pending in the application.

4a) Of the above claim(s) *33 and 50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8-22,26-28,32,35-44 and 46-49* is/are rejected.

7)☒ Claim(s) *7,23-25,29-31,34,45 and 51* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 September 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/18/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicants' election without traverse of Group II (claims 1-32, 34-49 and 51) in the reply filed on 7/18/2004 is acknowledged. Claims 1-51 are pending in the instant application. Claims 33 and 50 are withdrawn from consideration as being drawn to a nonelected embodiment.

Information Disclosure Statement

Receipt of an information disclosure statement, filed on 3/18/2004, is acknowledged. The signed and initialed PTO 1449 has been mailed with this action.

Specification

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: Vectors comprising a rat Kv2.1 polyadenylation sequence.

The disclosure is objected to because of the following informalities: Page 16, line 2 appears to contain a typographical error. The term "mb1" appears to be referring to the pMB1 origin of replication.

Appropriate correction is required.

Drawings

The drawings are objected to because Figures 1 and 2 are hand-drawn plasmid maps that may not reproduce well. Further, it is not clear from the drawings or the figure legends whether the box containing the term "Kv2.1" refers to only the polyadenylation sequence or to the entire gene or cDNA of rat Kv2.1. Corrected drawing sheets are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. The replacement sheet(s) should be labeled "Replacement Sheet" in the page header (as per 37 CFR 1.84(c)) so as not to obstruct any portion of the drawing figures. If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

In addition to Replacement Sheets containing the corrected drawing figure(s), applicant is required to submit a marked-up copy of each Replacement Sheet including annotations indicating the changes made to the previous version. The marked-up copy must be clearly labeled as "Annotated Marked-up Drawings" and must be presented in the amendment or remarks section that explains the change(s) to the drawings. See 37 CFR 1.121(d). Failure to

timely submit the proposed drawing and marked-up copy will result in the abandonment of the application.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11 and 26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 11 is indefinite in that the metes and bounds of the term "Tn917" are unclear. The claim is drawn to antibiotic resistance cassettes that confer resistance to an antibiotic selected from the group listed in the claim. The term "Tn917" is listed in the claim as an antibiotic. However, Tn917 is a type of transposon. It would be remedial to amend the claim to remove Tn917 from the list of antibiotics or to include the antibiotic to which an antibiotic resistance gene of Tn917 confers resistance.

Claim 26 is indefinite in that it depends from itself. It would be remedial to amend the claim to clearly indicate the claim from which it depends.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4-6, 8-11, 32, 35, 37-40, 42-44, 46, 47 and 49 are rejected under 35 U.S.C. 102(b) as being anticipated by Brock et al (J. Gen. Physiol., Vol. 118, pages 113-133, 2001; see the entire reference), as evidenced by the following references: Murakoshi and Trimmer (The Journal of Neuroscience, Vol. 19, No. 5, pages 1728-1735, 1999), Frech et al (Nature, Vol. 340, pages 642-645, 1989), Lee et al (The Journal of Biological Chemistry, Vol. 266, No. 18, pages 11448-11454, 1991), Short et al (Nucleic Acids Research, Vol. 16, No. 15, pages 7583-7600, 1988), REBASE version 001 (Richard J. Roberts, http://rebase.neb.com, 1999, see the selected entries).

Brock et al teach a plasmid vector comprising the rat Kv2.1 cDNA sequence in the pRBG4 vector (e.g. page 115, left column, paragraph 1). This vector was transfected into HEK 293 cells (e.g. Abstract; page 115, left column, paragraph 3; Figure 11).

Brock et al disclose that the Kv2.1 cDNA sequence in pRBG4 was provided by J.S. Trimmer (e.g. page 115, left column, paragraph 1). Murakoshi and Trimmer (e.g. page 1729, left column, *Transient transfection of COS-1 cells*) describe the rat Kv2.1 sequence in the pRBG4 vector as the full-length cDNA for Kv2.1 as disclosed by Frech et al. Frech et al disclose the full-length Kv2.1 cDNA sequence as capable of encoding the ion channel peptide and including the polyA sequence (e.g. page 643, paragraph bridging the left and right columns).

Lee et al constructed the pRBG4 vector by cloning the 740 bp BalI/SacII restriction fragment of the cytomegalovirus immediate early gene into the SacII and BamHI sites of Bluescript pSK M13+, using a synthetic oligonucleotide adapter (e.g. page 11449, *Construction*

of the Expression Vector). The Bluescript pSK vector is taught by Short et al (e.g. Figure 2). The resulting pRBG4 vector has the following features:

1. A cytomegalovirus (CMV) promoter (e.g. Lee et al, page 11449, *Construction of the Expression Vector*).

2. Multiple cloning sites, including HindIII, BamHI, BstI, KpnI, Asp718I, EcoRI, EcoRV, Eco32I, PstI, XhoI, and Sfr274I (e.g. Short et al, Figure 2). The recognition sequence of BstI is identical to that of BamHI (Roberts, see the entry for AacI). The recognition sequence of Asp718I is identical to that of KpnI (Roberts, see the entry for Acc65I). The recognition sequence of Eco32I is identical to that of EcoRV (Roberts, see the entry for Bsc217I). The recognition sequence of Sfr274I is identical to that of XhoI (Roberts, see the entry for AbrI).

3. An f1 origin of replication and a ColE1 origin of replication from pUC19 (e.g. Short et al, Figure 2; page 7585, *Construction of Bluescribe and Bluescript Phagemids*).

4. An ampicillin resistance gene (e.g. Short et al, Figure 2).

Thus, Brock et al necessarily teach the vectors and cells containing the vectors that meet the limitations of claims 1, 4-6, 8-11, 32, 35, 37-40, 42-44, 46, 47 and 49.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 9-12, 14-22, 27, 28, and 48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brock et al in view of the 1997 Invitrogen Catalog (see page 55).

The teachings of the Brock et al reference are described above and applied as before, except:

The Brock et al reference teaches the pRBG4 vector comprising the rat Kv2.1 cDNA sequence, including the polyadenylation sequence. Brock et al do not teach the subcloning of the rat Kv2.1 cDNA sequence into the pCR3.1 vector.

The 1997 Invitrogen Catalog teaches the pCR3.1 vector, comprising a ColE1 ori, an f1 ori, an ampicillin resistance cassette, a polylinker containing multiple cloning sites, and a kanamycin or neomycin resistance cassette containing an SV40 promoter, SV40 ori and a TK polyA sequence (page 55, right column). The pCR3.1 vector is capable of directing both sense and antisense expression of a cloned insert in eukaryotic cells (page 55, right column).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the teachings of Brock et al to subclone the rat Kv2.1 cDNA sequence into the pCR3.1

vector described in the 1997 Invitrogen Catalog because Brock et al teach the use of the plasmid vector comprising the Kv2.1 cDNA sequence to transfect eukaryotic cells and because the 1997 Invitrogen Catalog teaches the pCR3.1 vector as a eukaryotic expression vector. The skilled artisan would have been motivated to make such a modification in order to express both sense and antisense transcripts in a eukaryotic cell. Absent any evidence to the contrary, there would have been a reasonable expectation of success in modifying the teachings of Brock et al to include the pCR3.1 vector taught by the 1997 Invitrogen Catalog.

Claims 1-3, and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brock et al in view of Schorpp et al (Nucleic Acids Research, Vol. 24, No. 9, 1996; see the entire reference).

The teachings of the Brock et al reference are described above and applied as before, except:

The Brock et al reference teaches a vector comprising a CMV promoter, multiple cloning sites, f1 and ColE1 origins of replication, an ampicillin resistance gene, and the Kv2.1 cDNA sequence, including the polyadenylation sequence. Brock et al do not teach the use of a human ubiquitin promoter.

Schorpp et al teach the use of the human ubiquitin C (UbC) promoter to express heterologous genes in transgenic mice (e.g. Abstract; page 1787, left column, paragraph 4; page 1787, right column, paragraph 1). The UbC promoter is capable of directing transcription of the heterologous genes in a wider range of tissues than the CMV promoter (e.g. page 1787, right column, paragraph 2).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the teachings of the Brock et al reference to include the use of the UbC promoter taught by Schorpp et al because Brock et al teach the use of the CMV promoter to direct expression of an operably linked gene in mammalian cells and because Schorpp et al teach that the UbC promoter directs expression in mammalian cells. The skilled artisan would have been motivated to make such a modification in order to allow expression of the operably linked gene in a wider range of tissues as compared to the CMV promoter taught by Brock et al. Absent any evidence to the contrary, there would have been a reasonable expectation of success in modifying the teachings of Brock et al to include the pCR3.1 vector taught by the 1997 Invitrogen Catalog.

Claims 1, 9, 10, 13, and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brock et al in view of Izumi et al (Experimental Cell Research, Vol. 197, pages 229-233, 1991; see the entire reference).

The teachings of the Brock et al reference are described above and applied as before, except:

The Brock et al reference teaches a vector comprising a CMV promoter, multiple cloning sites, f1 and ColE1 origins of replication, an ampicillin resistance gene, and the Kv2.1 cDNA sequence, including the polyadenylation sequence. Brock et al do not teach the use of a blasticidin resistance gene.

Izumi et al teach a blasticidin resistance gene, *bsr*, which encodes an enzyme that converts the antibiotic blasticidin S to an inactive deaminohydroxy derivative (e.g. page 229,

paragraph bridging the columns). Izumi et al teach the use of the *bsr* gene operably linked to the SV40 early promoter (e.g. page 230, *Construction of pSV2bsr2*; Figure 2). The *bsr* gene confers resistance to blasticidin S in mammalian cells, allows the production of stable cell lines, and provides the benefit of being able to plate cells at high density without the need to change the medium as many times as compared to treatment of cells with G418 (e.g. page 232, *Analyses of Transfectants*; Figure 6; page 233, *Save Time Selection of bsr Transfectants*).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the teachings of Brock et al to include the use of the *bsr* gene operably linked to the SV40 early promoter as taught by Izumi et al because Brock et al teach the use of a vector to transfect mammalian cells and because Izumi et al teach the use of a dominant selectable marker for mammalian cells (i.e. the *bsr* gene). The skilled artisan would have been motivated to make such a modification in order to generate stable cell lines comprising the vector as exemplified by Izumi et al. Absent any evidence to the contrary, there would have been a reasonable expectation of success in modifying the teachings of Brock et al to include the *bsr* gene taught by Izumi et al.

Claims 1, 4, 9-11, and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brock et al in view of Drocourt et al (Nucleic Acids Research, Vol. 18, No. 13, page 4009, 1990; see the entire reference) as evidenced by (Richard J. Roberts, http://rebase.neb.com, 1999, see the selected entries).

The Brock et al reference teaches a vector comprising a CMV promoter, multiple cloning sites, f1 and ColE1 origins of replication, an ampicillin resistance gene, and the Kv2.1 cDNA

sequence, including the polyadenylation sequence. Brock et al do not teach the use of a phleomycin resistance gene or the use of the NdeI or FauNDI cloning sites.

Drocourt et al teach the Sh *ble* gene, which confers resistance to phyleomycins in prokaryotic and eukaryotic cells, and can be used as a selectable marker (e.g. page 4009, left column). Drocourt et al added synthetic oligomers with multiple cloning sites, including NdeI and FauNDI, to the Sh *ble* gene to facilitate cloning into vectors (e.g. page 4009, left column; Figure). The recognition sequence of FauNDI is identical to that of NdeI (Roberts, see the entry for FauNDI).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the teachings of Brock et al to include the use of the Sh *ble* gene taught by Drocourt et al because Brock et al teach the use of a vector to transfect mammalian cells and because Drocourt et al teach the use of the Sh *ble* gene as a resistance marker in eukaryotic cells. The skilled artisan would have been motivated to make such a modification in order to use the same selectable marker in prokaryotes and eukaryotes as taught by Drocourt et al. Absent any evidence to the contrary, there would have been a reasonable expectation of success in modifying the teachings of Brock et al to include the Sh *ble* gene taught by Drocourt et al.

Claims 1, 9-11, 35, 36, and 47 rejected under 35 U.S.C. 103(a) as being unpatentable over Brock et al in view of Kirschman et al (Gene, Vol. 68, pages 163-165, 1988; see the entire reference).

The Brock et al reference teaches a vector comprising a CMV promoter, multiple cloning sites, f1 and ColE1 origins of replication, an ampicillin resistance gene, and the Kv2.1 cDNA

sequence, including the polyadenylation sequence. Brock et al do not teach the use of a kanamycin or spectinomycin resistance genes or the transformation of the vector into a prokaryotic cell.

Kirschman et al teach two multi-purpose cloning vectors, pJKKmf(-) and pJKsp/Smf(-), that carry resistance to kanamycin and spectinomycin or streptomycin, respectively (e.g. abstract). Further, the vectors comprise a multiple cloning sites, the f1 and pBR322 origins of replication, and the T7 and SP6 promoters (e.g. Abstract; Figure 1). Kirschman et al teach the ligation of nucleotide sequences into the PstI site of the pJKKmf(-) vector followed by transformation of the vector into *E. coli* (e.g. page 165, (b) Rapid subcloning with pJKKmf(-)).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the teachings of Brock et al to subclone the rat Kv2.1 cDNA sequence into the vectors taught by Kirschman et al because Brock et al teach the use of a plasmid containing an ampicillin resistance gene for use in bacteria and because Kirschman et al teach the use of kanamycin and spectinomycin resistance genes in bacteria. The skilled artisan would have been motivated to make such a modification in order to have a choice of antibiotic resistance genes for selection of the plasmid in bacteria. Absent any evidence to the contrary, there would have been a reasonable expectation of success in modifying the teachings of Brock et al to include the Kv2.1 sequence operably linked to the CMV promoter in the vectors taught by Kirschman et al.

Conclusion

No claims are allowed. Claims 1-6, 8-22, 26-28, 32, 35-44, and 46-49 are rejected. Claims 7, 23-25, 29-31, 34, 45 and 51 are objected to as depending from a rejected claim. The

sequence search of SEQ ID NO: 2 did not identify any identical nucleic acid sequences in the commercial or interference databases.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Dunston whose telephone number is 571-272-2916. The examiner can normally be reached on M-F, 9 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR, http://pair-direct.uspto.gov) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

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Jennifer Dunston
Examiner
Art Unit 1636

GERRY LEFFERS
PRIMARY EXAMINER

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